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(2S,4S)-3-((1R)-1-hydroxyethyl)-2-azetidinone derivs. prodn. -
comprises reducing corresp. 3-acetyl deriv. in presence of NADP
oxido-reductase

Patent Assignee: MERCIAN CORP (SAOC)

Number of Countries: 001 Number of Patents: 002

✓Abstract (Basic): JP 4054182 A

Prodn. of (3S, 4S)-3((1R)-1-hydroxyethyl) -2-azetidinone derivs. of formula (I) comprises reducing (3S, 4S)-3-acetyl-2-azetidinone derivs. of formula (II) in presence of a NADP oxidoreductase produced by Streptomyces omiyaensis; where R1 and R2 = H, lower alkyl, phenyl, benzyl or diphenylmethyl, or together form lower alkylene; Z = H or amino-protecting gp.

The oxidoreductase is produced by Streptomyces omiyaensis W-4028 (FERM P-11210) isolated from the soil of Kumamoto Pref., Japan, which may be incubated in a medium contg. glycerol, meat extract, polypeptone, yeast extract, NaCl, MgSO₄.H₂O, CaHPO₄, CaCO₃ (precipitate), and defoaming agent, at 28 deg. C.

The redn. is carried out with the cells or their processed ones of Str. omiyaensis in an aq. medium (buffer soln.) at a temp. of 20-35 deg. C, pref. 25-30 deg. C, at pH 5-9, pref. pH 6-8, for a period of 3-48 hrs.. The prod. is extracted with a solvent, e.g. toluene, Et₂O, CHCl₃, EtOAc, BuOAc.

USE/ADVANTAGE - (I) are known as intermediates for beta-lactam antibiotics, e.g. formimidoylthienamycin (imipenem). The invention provides a new process for stereospecifically reducing (II) to (I) in high purity and high yield.

In an example, a soln. of 100 mg/ml (3S,4S)-3-acetyl-4-((1S)-2,2-dimethyl-1,3-dioxolan-4-yl)-1-(4-methoxyphenyl) -2-azetidinone in CHCl₃ (1 ml each) was placed in a 500 ml flask (x 3) and CHCl₃ was evapd. by blowing nitrogen gas to form thin film on the bottom of flask. Then, the cultured broth of Str. omiyaensis (250 ml each) was added and shaken at 28 deg. C for 24 hrs. n-BuOAc (50 ml) was added and the flask was shaken vigorously. The mixt. was centrifuged (2350 rpm, 10 mins, 10 deg. C) and the upper layer was washed with aq. NaCl, dried and evapd. to give 900 mg residue, which was chromatographed on a silica gel column (toluene/EtOAc=4/1) to give 333.9 mg (3S,4S)-3-((1R)-hydroxyethyl)-4-((1S)-2,2-dimethyl-1,3-dioxolan-4-yl)-1-(4-methoxyphenyl) -2-azetidinone.

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Title Terms: HYDROXYETHYL; AZETIDINONE; DERIVATIVE; PRODUCE; COMPRISE; REDUCE; CORRESPOND; ACETYL; DERIVATIVE; PRESENCE; NADP; OXIDO; REDUCTASE

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